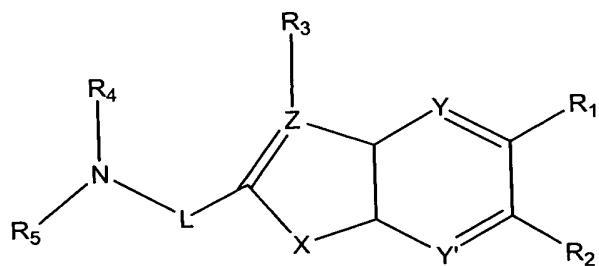
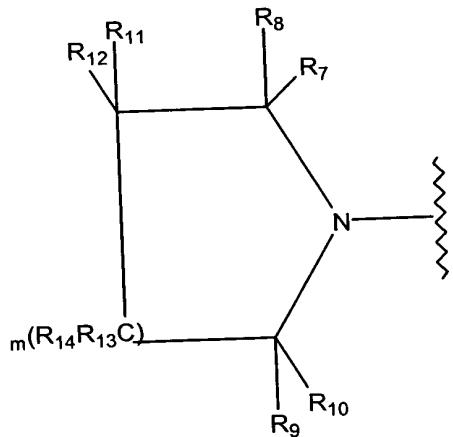


WHAT IS CLAIMED IS:

1. A compound of the formula:



5 or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein:
X is O, S, NH, or N(alkyl);
Y, and Y' are each independently selected from the group consisting of CH,
CF, and N;
10 Z is C or N, provided that when X is O or S, Z is N;
one of R₁ and R₂ is selected from the group consisting of aryl, heteroaryl, and
heterocycle;
the other of R₁ and R₂ is selected from the group consisting of hydrogen,
alkyl, alkoxy, aryl, cycloalkyl, halo, cyano, and thioalkoxy;
15 R₃ is absent when Z is N and, when present, R₃ is selected from the group
consisting of hydrogen, methyl, alkoxy, halo, and cyano;
R₄ and R₅ are each independently selected from the group consisting of alkyl,
haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, and cycloalkylalkyl, or R₄ and R₅
taken together with the nitrogen atom to which each is attached form a non-aromatic
20 ring of the structure (a):



(a) ;

$R_7, R_8, R_9,$ and R_{10} are each independently selected from the group consisting of hydrogen, hydroxyalkyl, fluoroalkyl, and alkyl; or one of the pair R_7 and R_8 or the pair R_9 and R_{10} is taken together to form a C_3-C_6 ring, wherein 0, 1, or 2 heteroatoms selected from O, N, or S replace a carbon atom in the ring;

5 R_{11} and R_{12} are each independently selected from the group consisting of hydrogen, hydroxy, hydroxyalkyl, alkyl, and fluoro;
 10 R_{13} and R_{14} at each occurrence are independently selected from the group consisting of hydrogen, alkyl, and fluoro;

15 L is $-[C(R_{15})(R_{16})]_n-$; R_{15} and R_{16} at each occurrence are independently selected from the group consisting of hydrogen, alkyl, alkoxy, and fluoro;

m is an integer from 0-3; and

20 n is an integer from 2-3.

2. The compound of claim 1, wherein R_1 is aryl or heteroaryl.

3. The compound of claim 1, wherein R_1 is heteroaryl.

20 4. The compound of claim 1, wherein R_1 and R_2 are each independently selected from the group consisting of furyl, imidazolyl, isoxazolyl, isothiazolyl,

oxadiazolyl, oxazolyl, nicotinyl, phenyl, pyrazinyl, pyrazolyl, pyridazinyl,
pyridazinonyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiadiazolyl, thiazolyl, thienyl,
triazinyl, triazolyl, azepanyl, azetidinyl, aziridinyl, azocanyl, morpholinyl, piperazinyl,
piperidinyl, pyrrolidinyl, pyrrolinyl, thiomorpholinyl, tetrahydrofuryl, tetrahydropyranlyl,
5 benzothienyl, isoquinolyl, indolyl, indolizin-2-yl, indazolyl, imidazo[1,2-a]pyridin-2-yl,
pyrazolo[1,5-a]pyridin-2-yl, 3-oxo-2H-pyridazin-2-yl, quinolyl, and 2-oxo-1H-pyridin-1-
yl.

5. The compound of claim 1, wherein R₁ is selected from the group consisting of
10 substituted phenyl, unsubstituted phenyl, substituted pyridine, and unsubstituted
pyridine.

6. The compound of claim 1, wherein R₁ is selected from the group consisting of
cyanophenyl, chlorophenyl, fluorophenyl, nicotinyl, pyridinyl, and quinolyl.

15 7. The compound of claim 1, wherein L is selected from the group consisting of -
CH₂CH₂- or -CH₂CH₂CH₂-

8. The compound of claim 1, wherein R₃ is hydrogen or methyl.

20 9. The compound of claim 1, wherein R₄ and R₅ taken together with the nitrogen
atom to which each is attached form a 4- to 7-membered non-aromatic ring
represented by formula (a).

25 10. The compound of claim 1, wherein the 4- to 7-membered non-aromatic ring is
selected from the group consisting of azepanyl, pyrrolidinyl, and piperidinyl.

11. The compound of claim 1, wherein at least one substituent represented by R₇,
R₈, R₉, and R₁₀ is selected from the group consisting of alkyl, halo, fluoroalkyl, and
30 hydroxyalkyl.

12. The compound of claim 1, wherein the 4- to 7-membered non-aromatic ring is selected from the group consisting of methylpyrrolidinyl, ethylpyrrolidinyl, dimethylaminopyrrolidinyl, isopropylpyrrolidinyl, isobutylpyrrolidinyl, hydroxymethylpyrrolidinyl, and fluoromethylpyrrolidinyl.

5

13. The compound of claim 1, wherein R₄ and R₅ are each independently selected from methyl, ethyl, and isopropyl.

10

14. The compound of claim 1, wherein at least one substituent represented by R₇, R₈, R₉, and R₁₀ is hydroxyalkyl, fluoroalkyl, or alkyl.

15. The compound of claim 1, wherein one substituent represented by R₇, R₈, R₉, and R₁₀ is methyl, ethyl, fluoromethyl, or hydroxymethyl.

15

16. The compound of claim 1, wherein one substituent represented by R₇, R₈, R₉, and R₁₀ is alkyl and the other three substituents are hydrogen.

17. The compound of claim 1, wherein R₁₁, R₁₂, R₁₃, and R₁₄ are each hydrogen.

20

18. The compound of claim 1, wherein R₁₃ and R₁₄ at each occurrence are each independently selected from the group consisting of hydrogen and alkyl.

19. The compound of claim 1, wherein R₁₅ and R₁₆ are hydrogen.

25

20. The compound of claim 1, wherein m is 0, 1, or 2.

21. The compound of claim 1, wherein n is 2.

22. The compound of claim 1, wherein X is O and Z is N.

30

23. The compound of claim 1, wherein X is -NH- or -N(alkyl)- and Z is C.

24. The compound of claim 1, wherein X is -NH- or -N(alkyl)- and Z is N.

25. The compound of claim 1, wherein X is S and Z is N.

5 26. The compound of claim 1, wherein:
R₁ is heteroaryl;
R₂ and R₃ are hydrogen;
L is -CH₂CH₂-;
m is 1; and
10 R₄ and R₅ are taken together to form a pyrrolidinyl ring of formula (a), wherein
one of R₇, R₈, R₉, and R₁₀ is methyl and the remaining three substituents are
hydrogen.

27. The compound of claim 26, wherein X is O or S and Z is N.

15 28. The compound of claim 1 selected from the group consisting of
4-[2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-5-yl]-benzonitrile;
4-[2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-5-yl]-benzonitrile;
3-[2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-p-tolyl-benzothiazole;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-m-tolyl-benzothiazole;
20 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-(4-Chloro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
5-(3-Chloro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
5-(4-Ethyl-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
Dimethyl-(4-{2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-5-yl}-
25 phenyl)-amine;
5-(4-Fluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
5-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-5-yl}-nicotinonitrile;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-6-pyridin-3-yl-benzothiazole;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-6-pyridin-4-yl-benzothiazole;
30 6-(6-Methoxy-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-
benzothiazole;

6-(3-Chloro-pyridin-4-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
6-(2,6-Difluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
5 2-Methyl-2'-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-[5,6']bibenzothiazolyl;
3-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-6-yl}-quinoline;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-6-pyrimidin-5-yl-benzothiazole;
6-(6-Fluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
10 5-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-benzothiazol-6-yl}-nicotinonitrile;
6-(1-Methyl-1H-indol-5-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
6-(2,6-Dimethyl-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzothiazole;
15 4-{2-[2-(2-methyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-[2-(2-Pyrrolidin-1-yl-ethyl)-benzooxazol-5-yl]-benzonitrile;
4-{2-[2-(2-(S)-methyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(3-(R)-Hydroxy-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
20 4-{2-[2-(2-(S)-Hydroxymethyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-(R),5-(R)-Dimethyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
benzonitrile;
25 4-[2-(2-Piperidin-1-yl-ethyl)-benzooxazol-5-yl]-benzonitrile;
4-{2-[2-(2-(R)-methyl-piperidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-(S)-Methoxymethyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
benzonitrile;
30 4-[2-(2-Azepan-1-yl-ethyl)-benzooxazol-5-yl]-benzonitrile;
4-[2-(2-Diethylamino-ethyl)-benzooxazol-5-yl]-benzonitrile;
4-{2-[2-(Isopropyl-methyl-amino)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(tert-Butyl-methyl-amino)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(Butyl-methyl-amino)-ethyl]-benzooxazol-5-yl}-benzonitrile;

4-{2-[2-(2-Hydroxymethyl-piperidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-Hydroxy-ethyl)-piperidin-1-yl]-ethyl}-benzooxazol-5-yl)-
benzonitrile;
4-{2-[2-(2-Isopropyl-pyrrolidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-(R)-Methyl-azetidin-1-yl)-ethyl]-benzooxazol-5-yl}-benzonitrile;
4-{2-[2-(2-(S)-Fluoromethyl-azetidin-1-yl)-ethyl]-benzooxazol-5-yl}-
benzonitrile;
4-{2-[2-(2-(S)-Hydroxymethyl-azetidin-1-yl)-ethyl]-benzooxazol-5-yl}-
benzonitrile;
4-[2-(2-Azetidin-1-yl-ethyl)-benzooxazol-5-yl]-benzonitrile;
4-(2-[2-[cis-2,6-dimethyl-piperidin-1-yl]-ethyl]-benzooxazol-5-yl)-benzonitrile;
4-(2-[2-[1,4,5,6-tetrahydropyrimidin-1-yl]-ethyl]-benzooxazol-5-yl)-benzonitrile;
4-(2-[2-[ethyl-isopropyl-amino]-ethyl]-benzooxazol-5-yl)-benzonitrile;
4-{2-[2-(2-methyl-propyl)-pyrrolidin-1-yl]-ethyl}-benzooxazol-5-yl}-
benzonitrile;
4-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-benzonitrile;
4-{1-Methyl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-
benzonitrile;
3-{1-Methyl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-
benzonitrile;
3-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-benzonitrile;
5-(4-Fluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole;
5-(3,5-Difluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-(4-trifluoromethoxy-phenyl)-1H-
indole;
2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-pyridin-3-yl-1H-indole;
1-(3-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-phenyl)-ethanone;
5-Furan-2-yl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole;
5-(2,6-Difluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole;
5-(6-Methoxy-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole;
5-(4-Methanesulfonyl-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
indole;

5-(2,6-Dimethyl-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 1-(4-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-phenyl)-ethanone; 5-(3-Fluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 5-(2,4-Dimethoxy-pyrimidin-5-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl)-Dimethyl-(4-{2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-phenyl)-amine; 5-(4-Chloro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 5-(2,4-Dimethoxy-pyrimidin-5-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-(3-trifluoromethyl-phenyl)-1H-indole; 2-Methyl-5-{2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-benzothiazole; 8-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-quinoline; 5-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-nicotinonitrile; 5-(5-Methoxy-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 5-(6-Fluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indole; 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-pyrimidin-5-yl-1H-indole; 1-Methyl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-5-pyridin-3-yl-1H-indole; 1-Methyl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-5-pyrimidin-5-yl-1H-indole; 5-{1-Methyl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-indol-5-yl}-nicotinonitrile; 4-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-benzonitrile; 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-pyridin-3-yl-1H-benzoimidazole; 5-(4-Fluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazole; 1-(4-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-phenyl)-ethanone; 3-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-benzonitrile; 1-(3-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-phenyl)-ethanone;

5-(3-Methoxy-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
5-Furan-2-yl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazole;
5-(2,6-Difluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-

5 benzoimidazole;
5-(6-Methoxy-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
5-(4-Methanesulfonyl-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
10 5-(2,4-Dimethoxy-pyrimidin-5-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
5-Benzo[1,3]dioxol-5-yl-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
5-(5-Methoxy-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
15 benzoimidazole;
5-(2,6-Dimethyl-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
4-{2-[2-(2-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-benzoic acid
methyl ester;
20 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-(4-methylsulfanyl-phenyl)-1H-
benzoimidazole;
5-(3,5-Difluoro-phenyl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole;
25 2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-5-pyrimidin-5-yl-1H-benzoimidazole;
8-{2-[2-(2-(R)-Methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-quinoline;
Dimethyl-(4-{2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-benzoimidazol-5-yl}-
phenyl)-amine; and
5-(6-Fluoro-pyridin-3-yl)-2-[2-(2-(R)-methyl-pyrrolidin-1-yl)-ethyl]-1H-
benzoimidazole.

30 29. A pharmaceutical composition comprising a therapeutically effective amount
of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

30. A method of selectively modulating the effects of histamine-3 receptors in a mammal comprising administering an effective amount of a compound of claim 1.

5 31. A method of treating a condition or disorder modulated by the histamine-3 receptors in a mammal comprising administering an effective amount of a compound of claim 1.

10 32. The method according to claim 31, wherein the condition or disorder is selected from the group consisting of acute myocardial infarction, Alzheimer's disease, asthma, attention-deficit hyperactivity disorder, bipolar disorder, cognitive enhancement, cognitive deficits in psychiatric disorders, deficits of memory, deficits of learning, dementia, cutaneous carcinoma, drug abuse, diabetes, type II diabetes, depression, epilepsy, gastrointestinal disorders, inflammation, insulin resistance syndrome, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, metabolic syndrome, mild cognitive impairment, migraine, mood and attention alteration, motion sickness, narcolepsy, neurogenic inflammation, obesity, obsessive compulsive disorder, pain, Parkinson's disease, polycystic ovary syndrome, schizophrenia, seizures, septic shock, Syndrome X, Tourette's syndrome, vertigo, and wakefulness.

15

20

33. The method according to claim 30, wherein the condition or disorder affects the memory or cognition.